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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,375	KATO ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26,40 and 42-50* is/are pending in the application.

4a) Of the above claim(s) *1-7,14-26 and 46-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13,40 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Action is in response to the communication filed on 3/15/04. Claims 1-26, 40 and 42-50 are pending in the application and are addressed herein.

Election/Restrictions

2. Applicant's election without traverse of Group II (claims 8-13, 40 and 42-45) as well as the indicated subgroups (2, G, a) and the indicated species (viii, i and i) as indicated in the paper filed 3/15/04, is acknowledged.

3. Claims 1-7 14-26 and 46-50 (as well as the non-elected subgroups and species) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, subgroup, or species; there being no allowable generic or linking claim. Election was made **without** traverse in the paper filed 3/15/04.

Claim Objections

4. Claims 40 and 42-45 are objected to because of the following reasons: Claims 40, 42 and 44, as currently written, depend on "any one of claims 1 to 13". However, claims 1-7 have been withdrawn from consideration as being drawn to a non-elected invention. The claims should be re-written to be dependent on only elected claims. It is noted that claims 43 and 45 are claims that depend on claims 42 and 44, respectively. Therefore, claims 43 and 45 are objected to for the same reason.

5. In the interest of compact prosecution, the instant claims will be interpreted as depending only elected claims (i.e., any one of claims 8-13).

Claim Rejections - 35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 8-13, 40 and 42-45 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The instant claims are drawn to a composition for gene therapy used for treating a disease susceptible to gene therapy, which contains as active ingredients an effective amount of a functional substance having an affinity for a virus that contains a gene useful for gene therapy and an effective amount of another functional substance having an affinity specific for a target cell for which transfer of the gene is required. It is clear that the claim is a composition for gene therapy (as indicated in the preamble of the claim); however, carefully reading the claim it appears that the claim only absolutely required 2 elements: 1) a functional substance having an affinity for a virus that contains a gene useful for gene therapy; and 2) another functional substance having an affinity specific for a target cell for which transfer of the gene is required. The claim does not explicitly require virus that contains a gene useful for gene therapy, only a functional substance that has affinity for the virus. As such, the omitted elements are: a virus that expresses a gene useful for gene therapy. Specifically, since the claim is a composition for gene therapy, it must contain all elements essential for gene therapy. In the instant claim a virus that expresses a gene useful for gene therapy is absolutely required in order to have a composition for gene therapy.

In the interest of compact prosecution, the claims will be interpreted as having all essential matter.

8. Additionally, claim 42 recites the limitation "the transferred gene" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim as none of claim 8-13 specifically recite [a/the] transferred gene. Claims 43-45 depend on claim 42 and are rejected for the same reason.

In the interest of compact prosecution, the claims will be interpreted as reading on "the gene useful for gene therapy" rather than "the transferred gene", thus allowing the phrase to have antecedent basis.

Claim Rejections - 35 USC § 112, first paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 8-13, 40 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a composition for gene therapy used for treating a disease susceptible to gene therapy, which contains as active ingredients an effective amount of a functional substance having an affinity for a virus that contains a gene useful for gene therapy

and an effective amount of another functional substance having an affinity specific for a target cell for which transfer of the gene is required (emphasis added). Therefore, the claims encompass a composition comprising two different functional substances, one having an affinity for a virus and the other having affinity for a specific target cell. As such, the claims encompass a composition that comprises two different molecules wherein each molecule is a species member of a large genus group. Specifically, the claims encompass a genus of molecules that have an affinity for a virus and a separate genus of molecules that have an affinity for a specific target cell.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164).

In the instant case, the claims encompass two different genuses of functional elements. Looking to the specification for guidance, the specification has described several different broad classes of molecules which have affinity for a virus, including anti-virus antibodies, heparin II binding domain of fibronectin, FGF, collagen and polylysine. However, these broad classes are not structurally related to each other. Therefore, there is no structure common to all members of the genus of molecules. Therefore, although the specification has adequately described specific subgroups of molecules that have an affinity for a virus wherein the subgroups are an anti-virus

antibody, heparin-II-binding domain of fibronectin, FGF, collagen and polylysine; the specification has not adequately described a representative number of species molecules of the genus because applicants have not clearly described the common structures that are critical to the function of each genus member. That is, no structure-function relationship has been disclosed such that other species molecules that belong to the genus could be readily identifiable. Furthermore, the claims encompass a large genus of viruses and there is no disclosure indicating which molecule has affinity for which specific virus.

Similarly, the specification has adequately described specific subgroups of molecules that have an affinity for a specific target cell including proteins having affinity for the target cell, hormones, cytokines, anti-target cell antibodies, sugar chains, carbohydrates and cells. However, these broad classes are not structurally related to each other. Therefore, there is no structure common to all members of the genus of molecules. Therefore, although the specification has adequately described specific subgroups of molecules that have an affinity for a specific target cell, it has not adequately described a representative number of species molecules of the genus because applicants have not clearly described the common structures that are critical to the function of each genus member. That is, no structure-function relationship has been disclosed such that other species molecules that belong to the genus could be readily identifiable. Furthermore, the claims encompass a large genus of target cells and there is no disclosure indicating which molecule(s) have affinity for which specific target cell.

It is noted that amending the claim such that the composition encompasses a specific molecule (such as heparin-II-binding domain of fibronectin) that has affinity for a specific virus

(such as a retrovirus) and another specific molecule (such as an vascular endothelial cell) that has affinity for a specific target cell-type (such as leukemia) would obviate this rejection.

11. Claims 8-13, 40 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> A gene therapy composition for inhibiting the growth of leukemia cells, wherein the composition contains as active ingredients:
>
> a) an effective amount of heparin-II-binding domain of fibronectin having affinity for a retrovirus that contains an anti-tumor gene; and
>
> b) an effective amount of a vascular endothelial cell having affinity specific for a said leukemia cell

does not reasonably provide enablement for the full scope encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a composition for gene therapy.

The breadth of the claims

As currently written, the claims are very broad and encompass a composition for treating (i.e., completely eliminating and/or preventing any future occurrence of) any disease that is susceptible to gene therapy wherein the composition can comprise 1) any one of a huge number of different molecules that have affinity for any gene therapy virus, and 2) any one of a huge number of different molecules that have affinity for the preferred target cell (which could be any one of a huge number of different target cells).

The unpredictability of the art and the state of the prior art

As indicated above, the claims are very broad, and in general, encompass a gene therapy composition for treating any disease susceptible to gene therapy. It is respectfully pointed out that "treating" encompasses completely eliminating (i.e., curing) as well as preventing any future occurrence of the disease. Scanning the prior art, no references can be found that indicate gene therapy can be effective for either 100% curing and/or 100% preventing a disease. With respect to the molecules that have affinity for a gene therapy virus, the elected subgroup is heparin-II-binding domain of fibronectin. The prior art appears to indicate the heparin-II-binding domain of fibronectin was known as a molecule that had an affinity for retroviral vectors, and could be useful for helping the retroviral vector infect a target cell, such as a hematopoietic cell (e.g., see Williams WO 97/11604). However, there is no indication in the prior art that heparin-II-binding domain of fibronectin has affinity for any other virus other than retrovirus.

Furthermore, with respect to the molecules that have affinity for specific target cells, it is noted that the elected subgroup is vascular endothelial cells. It appears that the notion of vascular endothelial cells having affinity for a specific target cell was known (e.g., see Juneja et

al. Experimental Hematology, 1992). However, it appears that the prior art only recognizes that vascular endothelial cells have affinity for leukemia cells (L1210). There is no indication in the prior art that vascular endothelial cells have affinity for any other cell types.

Working Examples and Guidance in the Specification

With respect to the elected invention (including the elected groups , subgroups and species), the specification describes a working example (see example 4) wherein a heparin-II-binding domain of fibronectin (specifically, the commercially available RetroNectin) was used a molecule having affinity for a retroviral vector that expresses GFP and HUVECs (vascular endothelial cells) were used as cells having affinity for a specific target cell-type (L1210, leukemia cells). When the two functional substances were incubated, first with retrovirus that expresses GFP, and then with L1210 cells, the results indicate that the nucleic acid encoding GFP is transferred into and expressed in the target L1210 cells (see Example 4).

Quantity of Experimentation

Considering the breadth of the claims, as indicated above, as well as the fact that the claims encompass 2 genuses of molecules which have not been adequately described. Additional experimentation is required in order for one of skill in the art to be able to make and use the claimed invention to the full scope encompassed by the claims. For instance, additional experimentation would be required to determine which molecules had affinity for which specific viruses. As well as which molecules have affinity for which specific target cells. It is noted that the additional experimentation required with respect to these molecules would be not to determine which individual molecules had the desired affinity, but to identify a representative number of molecules that belong to each genus. Furthermore, additional experimentation would

need to be performed in order to determine if the heparin-II-binding domain of fibronectin has affinity for any virus other than retrovirus, and to determine if vascular endothelial cells have affinity for any cells other than L1210 cells.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the breadth of the claims, the limited knowledge of the art, the limited amount of working examples and guidance in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed invention is undue.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 8-11, 40, 42-45 rejected under 35 U.S.C. 102(b) as being anticipated by Jolley et al. (WO 95/31566, cited in I.D.S. as reference AE).

The instant claims are drawn to a composition for gene therapy used for treating a disease susceptible to gene therapy, which contains as active ingredients an effective amount of a functional substance having an affinity for a virus that contains a gene useful for gene therapy

and an effective amount of another functional substance having an affinity specific for a target cell for which transfer of the gene is required (claim 8); wherein the composition comprises an effective amount of the virus that contains a gene useful for gene therapy (claim 9); wherein the functional substance having an affinity for a virus is heparin-II-binding domain of fibronectin (claim 10); wherein the functional substance having an affinity for a specific target cell is selected from the group consisting of proteins each having an affinity for the target cell, hormones, cytokines, anti-target cell antibodies, sugar chains, carbohydrates, and cells (claim 11, note: the elected subgroup=cells); wherein the target cell is a cancer cell (claim 40); wherein a protein encoded by the gene useful for gene therapy is expressed in the target cell in an amount sufficient for treatment (claim 42); wherein the protein is an enzyme (claim 43); wherein the virus is a virus vector (claim 44); wherein the virus is a retrovirus vector (claim 45).

Jolley teaches a composition and method for targeting gene delivery vehicles wherein the composition comprises a first element (a) that is a targeting element that has affinity for a selected cell type (including a cancer cell) in a warm-blooded animal, and second element (b) that has high affinity for a gene delivery vehicle (e.g., see abstract). It is noted that Jolley teaches that the first element (a) specifically binds to the second element (b) (e.g., see abstract); however, there is no limitation in the instant claims that the two elements cannot specifically bind to each other. Jolley teaches that the second element (b), which has affinity for a gene delivery vehicle, is heparin-II-binding domain of fibronectin. Jolley also that the gene delivery vehicle can be a retrovirus vector that encodes an anti-tumor protein such as the enzyme HSVTK. Although Jolley does not teach a first element (a) that has affinity for a target cell is a cell (the elected subgroup), it is noted that claims 8-10, 40 and 42-45 are broad claims that do not

explicitly contain this limitation. As such, Jolley anticipates the broad claims 8-10, 40 and 42-45. Regarding claim 11, although Jolley does not teach that the element that has affinity for the target cell is a cell (the elected subgroup), Jolley does teach that the element that has affinity for the target cell can be an anti-target cell antibody (explicitly claimed in claim 11). As such, Jolley anticipates instant claim 11. (Please see: abstract; page 2, line 18 through page 4, line 19; and page 5, line 36 through page 10, line 29 for Jolley's teachings of the above indicated material).

14. Claims 8-13, 40 and 42-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams (WO 97/11604).

The instant claims are drawn to a composition for gene therapy used for treating a disease susceptible to gene therapy, which contains as active ingredients an effective amount of a functional substance having an affinity for a virus that contains a gene useful for gene therapy and an effective amount of another functional substance having an affinity specific for a target cell for which transfer of the gene is required (claim 8); wherein the composition comprises an effective amount of the virus that contains a gene useful for gene therapy (claim 9); wherein the functional substance having an affinity for a virus is heparin-II-binding domain of fibronectin (claim 10); wherein the functional substance having an affinity for a specific target cell is selected from the group consisting of proteins each having an affinity for the target cell, hormones, cytokines, anti-target cell antibodies, sugar chains, carbohydrates, and cells (claim 11, note: the elected subgroup=cells); wherein the substance having affinity for the target cell is a cell having affinity for the target cell (claim 12); wherein the substance having affinity for the

target cell is a cell selected from group consisting of: vascular endothelial cells, inflammatory cells, hematopoietic stem cells, brain endothelial cells and bone marrow cells (claim 13, note the elected subgroup=vascular endothelial cells); wherein the wherein the target cell is a cell selected from the group consisting of hematopoietic stem cells, blood cells, leukocytes, lymphocytes, T cells, tumor-infiltrating lymphocytes, B cells, and cancer cells (claim 40); wherein a protein encoded by the gene useful for gene therapy is expressed in the target cell in an amount sufficient for treatment (claim 42); wherein the protein is an enzyme (claim 43); wherein the virus is a virus vector (claim 44); wherein the virus is a retrovirus vector (claim 45).

Williams teaches a method for increasing the efficiency of transduction of hematopoietic stem cells with retroviruses encoding a gene useful for gene therapy (the ADA gene, which encodes an enzyme), using the heparin-II-binding domain of fibronectin--which has affinity for the retrovirus (e.g., see abstract; page 1; lines 24-29; page 2, lines 4-10; paragraph bridging pages 5-6; page 7, lines 15-19; page 26 lines 7-17). As such, Williams teaches a composition that comprises all of the elements indicated in the claims, including: a retroviral vector that encodes an enzyme (ADA) useful for gene therapy, a first substance that is heparin-II-binding domain of fibronectin which has affinity for the retrovirus, and a second functional substance that is a hematopoietic stem cell (e.g., see Examples 7 and 10 in Williams). It is noted that Williams does not teach that the substance having affinity for the target cell is a vascular endothelial cell (the elected subgroup). However, claim 13 also indicates that that the substance having affinity for the target cell can be hematopoietic stem cells and claim 40 indicates that the target cell can be a hematopoietic stem cell. As such, Williams anticipates the instant claims as they are drawn to a composition comprising a retroviral vector encoding an enzyme, heparin-II-binding domain of

fibronectin and hematopoietic stem cells. It is noted that hematopoietic stem cells would necessarily have affinity for target cells, such as other hematopoietic cells as clearly indicates in the specification and instant claims (e.g., see claims 13 and 40).

Furthermore it is respectfully pointed out that the instant claims are drawn to a product (a composition) and not a method of use the product. As such, any functional language in the claims does not bear patentable weight and the only requirement necessary to anticipate the instant claims is a composition comprising all of the claimed elements.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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